Notice of Allowability	Application No.	Applicant(s)
	10/566,432	MARAHIEL ET AL.
	Examiner	Art Unit
	Susan E. Fernandez	1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *telephone interview with applicant's representative on 7/15/11*.
2. ☒ The allowed claim(s) is/are *1-14 and 17*.
3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☒ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☒ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)	5. ☐ Notice of Informal Patent Application
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)	6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *20110715* .
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____	7. ☒ Examiner's Amendment/Comment
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material	8. ☒ Examiner's Statement of Reasons for Allowance
	9. ☐ Other _____.

/Allison M. Ford/
Primary Examiner, Art Unit 1653

EXAMINER'S AMENDMENT

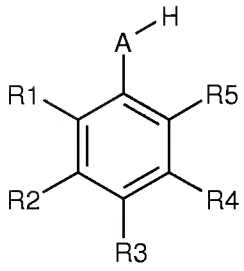
An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Christopher Brody on July 15, 2011.

The application has been amended as follows:

Claim 5 is **amended** as follows:

Claim 5. The method for the production of cyclic peptides according to claim 1, wherein the charge-stabilized leaving group is a compound of the formula



(I)

wherein the following applies:

A is selected from O [[or]] and S,

and whereby R1, R2, R3, R4 and R5 are independent of one another and are selected from:

$-NO_2$, -CN, -F, -Cl, -Br, -I, $-CH_2Cl$, $-SO_3H$, -H, $-NH_3^+$, $-NL_3^+$, -C(=O)L, -C(=O)Het, $-O^-$, $-NL_2$, $-NH_2$, -OL, -OH, -NHC(=O)L,

-OC(=O)L, -SL, $-CO_2^-$, -alkyl, -alkenyl, -cycloalkyl,

-cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl, and

-heteroaryl,

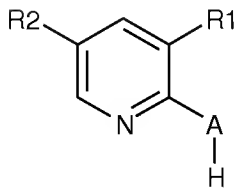
wherein

L is selected from: -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl,

-heteroalkyl, -heterocycloalkyl, -aryl, and -heteroaryl, wherein -alkyl stands for a group with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated group with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -cycloalkyl and –cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl stands for an alkyl group wherein up to 5 carbon atoms are substituted by atoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; the heterocyclic group stands for a residue with 1 to 20 carbon atoms wherein up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, phosphorus; aryl stands for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a corresponding aromatic residue in which up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus.

Claim 6 is **amended** as follows:

Claim 6. The method ~~Method~~ for the production of cyclic peptides according to claim 1, wherein the charge-stabilized leaving group is a compound of the formula



(II)

wherein the following applies:

A [[= O, S]] is selected from O and S

and whereby R1 and R2 are independent of one another and are selected from:

$-NO_2$, -CN, -F, -Cl, -Br, -I, $-CH_2Cl$, $-SO_3H$, -H, $-NH_3^+$, $-NL_3^+$, -C(=O)L, -C(=O)Het, $-O^-$, $-NL_2$, $-NH_2$, -OL, -OH, -NHC(=O)L, -OC(=O)L, -SL, $-CO_2^-$, -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl, and

-heteroaryl,

wherein

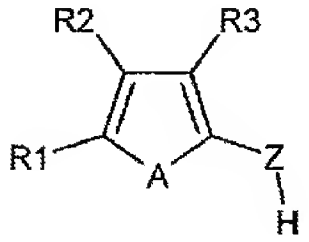
L [[=]] is selected from -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl,

-heteroalkyl, -heterocycloalkyl, -aryl, and -heteroaryl, wherein -alkyl stands for a group with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated group with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -cycloalkyl and –cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl stands for an alkyl group wherein up to 5 carbon atoms are substituted by atoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; the heterocyclic groups stand for a residue with 1 to 20 carbon atoms wherein up to

5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; aryl stands for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a corresponding aromatic residue in which up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus.

Claim 7 is **amended** as follows:

Claim 7. The method ~~Method~~ for the production of cyclic peptides according to claim 1, wherein the charge-stabilized leaving group is a compound of the formula



(III)

wherein the following applies:

A [[= O, S]] is selected from O and S and

Z [[= O, S,]] is selected from O and S,

and whereby R1, R2, and R3 are independent of one another and are selected from:

$-NO_2$, -CN, -F, -Cl, -Br, -I, $-CH_2Cl$, $-SO_3H$, -H, $-NH_3^+$, $-NL_3^+$, -C(=O)L, -C(=O)Het, $-O^-$, $-NL_2$, $-NH_2$, -OL, -OH, -NHC(=O)L, -OC(=O)L, -SL, $-CO_2^-$, -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl, and

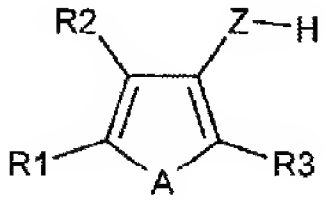
-heteroaryl,

wherein

L [[=]] is selected from -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl, and -heteroaryl, wherein -alkyl stands for a group with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated group with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -cycloalkyl and –cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl stands for an alkyl group wherein up to 5 carbon atoms are substituted by atoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; the heterocyclic groups stand for a residue with 1 to 20 carbon atoms wherein up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; aryl stands for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a corresponding aromatic residue in which up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus.

Claim 8 is **amended** as follows:

Claim 8. The method ~~Method~~ for the production of cyclic peptides according to claim 1, wherein the charge-stabilized leaving group is a compound of the formula



(IV)

wherein the following applies:

A [[= O, S]] is selected from O and S and

Z [[= O, S,]] is selected from O and S,

and whereby R1, R2, and R3 are independent of one another and are selected from:

$-NO_2$, -CN, -F, -Cl, -Br, -I, $-CH_2Cl$, $-SO_3H$, -H, $-NH_3^+$, $-NL_3^+$, -C(=O)L, -C(=O)Het, $-O^-$, $-NL_2$, $-NH_2$, -OL, -OH, -NHC(=O)L, -OC(=O)L, -SL, $-CO_2^-$, -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl, and

-heteroaryl,

wherein

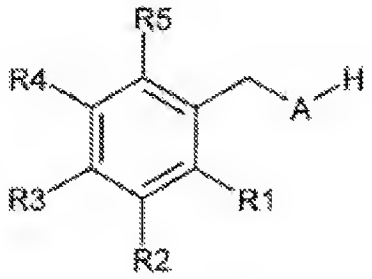
L [[=]] is selected from -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl,

-heteroalkyl, -heterocycloalkyl, -aryl, and -heteroaryl, wherein -alkyl stands for a group with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated group with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -cycloalkyl and –cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl stands for an alkyl group wherein up to 5 carbon atoms are substituted by atoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; the heterocyclic groups stand for a residue with 1 to 20 carbon atoms wherein up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; aryl stands for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a corresponding aromatic residue in which up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus.

Claim 9 is **amended** as follows:

Claim 9. The method ~~Method~~ for the production of cyclic peptides according to claim 1,

wherein the charge-stabilized leaving group is a compound of the formula



(V)

wherein the following applies:

A [[= O, S]] is selected from O and S

and whereby R1, R2, R3, R4 and R5 are independent of one another and are selected from:

$-NO_2$, -CN, -F, -Cl, -Br, -I, $-CH_2Cl$, $-SO_3H$, -H, $-NH_3^+$, $-NL_3^+$, -C(=O)L, -C(=O)Het, $-O^-$, $-NL_2$, $-NH_2$, -OL, -OH, -NHC(=O)L, -OC(=O)L, -SL, $-CO_2^-$, -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl, and -heteroaryl,

wherein

L [[=]] is selected from -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl, and -heteroaryl, wherein -alkyl stands for a group with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated group with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -cycloalkyl and –cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl stands for an alkyl group wherein up to 5

carbon atoms are substituted by atoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; the heterocyclic groups stand for a residue with 1 to 20 carbon atoms wherein up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; aryl stands for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a corresponding aromatic residue in which up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus.

Claim 10 is **amended** as follows:

Claim 10. Method for the production of a substrate and subsequent reaction of this substrate with peptide cyclases into a cyclic peptide, wherein the substrate is a linear peptide ~~substrates are linear peptides~~, wherein the following steps are carried out one after the other:

[[-]] adding to a free peptide acid in a solvent a reagent activating the C-terminus of the peptide acid, a coupling additive and a charge-stabilized to obtain a mixture ~~leaving group to the free peptide acid in a solvent~~,

[[-]] stirring the mixture at room temperature,

[[-]] adding [[of]] a base to the mixture and further stirring the mixture at room temperature,

[[-]] filtering the mixture,

[[-]] removing [[of]] the solvent from the mixture,

[[-]] deprotecting [[of]] the linear peptide resulting from the previous steps,

[[-]] adding [[of]] a peptide cyclase to the linear peptide, and

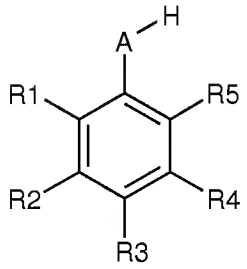
[[-]] purifying [[of]] the cyclic peptide obtained.

[[-]] wherein an acyl group of the C-terminal free peptide acid of the linear peptide is bound to the charge-stabilized leaving group.

Claim 11 is **amended** as follows:

Claim 11. The method~~Method~~ for the production of a substrate and subsequent reaction of this substrate with peptide cyclases into a cyclic peptide according to claim 10, wherein the acyl group of the C-terminal amino acid of the linear peptide is bound to one of the charge-stabilized leaving groups selected from the following:

a.) a compound of the formula



(I)

wherein the following applies:

A [[= O, S]] is selected from O and S,

and whereby R1, R2, R3, R4 and R5 are independent of one another and are selected from:

$-NO_2$, -CN, -F, -Cl, -Br, -I, $-CH_2Cl$, $-SO_3H$, -H, $-NH_3^+$, $-NL_3^+$, -C(=O)L, -C(=O)Het, $-O^-$, $-NL_2$, $-NH_2$, -OL, -OH, -NHC(=O)L,

-OC(=O)L, -SL, $-CO_2^-$, -alkyl, -alkenyl, -cycloalkyl,

-cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl, and

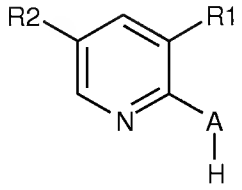
-heteroaryl,

wherein

L [[=]] is selected from: -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl,

-heteroalkyl, -heterocycloalkyl, -aryl, and -heteroaryl, wherein -alkyl stands for a group with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated group with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -cycloalkyl and –cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl stands for an alkyl group wherein up to 5 carbon atoms are substituted by atoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; the heterocyclic group stands for a residue with 1 to 20 carbon atoms wherein up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; aryl stands for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a corresponding aromatic residue in which up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus;

(b) a compound of the formula



(II)

wherein the following applies:

A [[= O, S]] is selected from O and S

and whereby R1 and R2 are independent of one another and are selected from:

$-NO_2$, -CN, -F, -Cl, -Br, -I, $-CH_2Cl$, $-SO_3H$, -H, $-NH_3^+$, $-NL_3^+$, -C(=O)L, -C(=O)Het, $-O^-$, $-NL_2$, $-NH_2$, -OL, -OH, -NHC(=O)L, -OC(=O)L, -SL, $-CO_2^-$, -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl, and

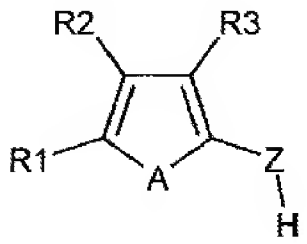
-heteroaryl,

wherein

L [[=]] is selected from -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl,

-heteroalkyl, -heterocycloalkyl, -aryl, and -heteroaryl, wherein -alkyl stands for a group with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated group with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -cycloalkyl and –cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl stands for an alkyl group wherein up to 5 carbon atoms are substituted by atoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; the heterocyclic groups stand for a residue with 1 to 20 carbon atoms wherein up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; aryl stands for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a corresponding aromatic residue in which up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus;

(c) a compound of the formula



(III)

wherein the following applies:

A [[= O, S]] is selected from O and S and

Z [[= O, S,]] is selected from O and S,

and whereby R1, R2, and R3 are independent of one another and are selected from:

$-NO_2$, -CN, -F, -Cl, -Br, -I, $-CH_2Cl$, $-SO_3H$, -H, $-NH_3^+$, $-NL_3^+$, -C(=O)L, -C(=O)Het, $-O^-$, $-NL_2$, $-NH_2$, -OL, -OH, -NHC(=O)L, -OC(=O)L, -SL, $-CO_2^-$, -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl, and

-heteroaryl,

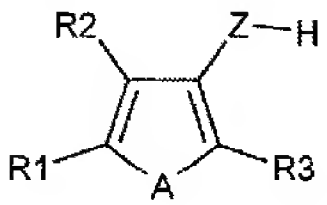
wherein

L [[=]] is selected from -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl,

-heteroalkyl, -heterocycloalkyl, -aryl, and -heteroaryl, wherein -alkyl stands for a group with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated group with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -cycloalkyl and –cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl stands for an alkyl group wherein up to 5 carbon atoms are substituted by atoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; the heterocyclic groups stand for a residue with 1 to 20 carbon atoms wherein up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur,

and phosphorus; aryl stands for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a corresponding aromatic residue in which up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus;

(d) a compound of the formula



(IV)

wherein the following applies:

A [[= O, S]] is selected from O and S and

Z [[= O, S,]] is selected from O and S,

and whereby R1, R2, and R3 are independent of one another and are selected from:

$-NO_2$, -CN, -F, -Cl, -Br, -I, $-CH_2Cl$, $-SO_3H$, -H, $-NH_3^+$, $-NL_3^+$, -C(=O)L, -C(=O)Het, $-O^-$, $-NL_2$, $-NH_2$, -OL, -OH, -NHC(=O)L, -OC(=O)L, -SL, $-CO_2^-$, -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl, and

-heteroaryl,

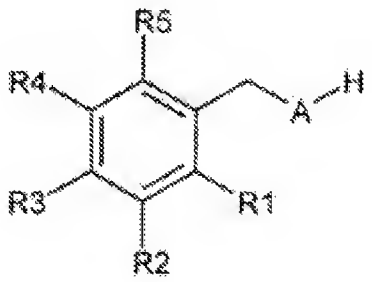
wherein

L [[=]] is selected from -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl,

-heteroalkyl, -heterocycloalkyl, -aryl, and -heteroaryl, wherein -alkyl stands for a group with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated group with 2 to 20

carbon atoms and -alkyl or -alkenyl are linear or branched; -cycloalkyl and –cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl stands for an alkyl group wherein up to 5 carbon atoms are substituted by atoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; the heterocyclic groups stand for a residue with 1 to 20 carbon atoms wherein up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; aryl stands for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a corresponding aromatic residue in which up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; and

(e) a compound of the formula



(V)

wherein the following applies:

A [[= O, S]] is selected from O and S

and whereby R1, R2, R3, R4 and R5 are independent of one another and are selected from:

$-NO_2$, -CN, -F, -Cl, -Br, -I, $-CH_2Cl$, $-SO_3H$, -H, $-NH_3^+$, $-NL_3^+$, -C(=O)L, -C(=O)Het, $-O^-$, $-NL_2$, $-NH_2$, -OL, -OH, -NHC(=O)L, -OC(=O)L, -SL, $-CO_2^-$, -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl, and -heteroaryl,

wherein

L [[=]] is selected from -alkyl, -alkenyl, -cycloalkyl, -cycloalkenyl, -heteroalkyl, -heterocycloalkyl, -aryl, and -heteroaryl, wherein -alkyl stands for a group with 1 to 20 carbon atoms and -alkenyl for a monounsaturated or polyunsaturated group with 2 to 20 carbon atoms and -alkyl or -alkenyl are linear or branched; -cycloalkyl and –cycloalkenyl stand for a group with 3 to 20 carbon atoms; heteroalkyl stands for an alkyl group wherein up to 5 carbon atoms are substituted by atoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; the heterocyclic groups stand for a residue with 1 to 20 carbon atoms wherein up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus; aryl stands for an aromatic residue with 5 to 20 carbon atoms and heteroaryl stands for a corresponding aromatic residue in which up to 5 carbon atoms are substituted by heteroatoms chosen from the group nitrogen, oxygen, sulfur, and phosphorus.

Claim 12 is **amended** as follows:

Claim 12. The method ~~Method~~ for the production of a substrate and subsequent reaction of this substrate with peptide cyclases into a cyclic peptide according to claim 11, wherein the leaving group possesses a pK_A value less than or equal to 10, preferably less than or equal to 8.

Claim 13 is **amended** as follows:

Claim 13. The method ~~Method~~ for the production of a substrate and subsequent reaction of this substrate with peptide cyclases into a cyclic peptide according to claim 10, wherein DCC (dicyclohexylcarbodiimide), DCI (N,N-diisopropylcarbodiimide), PyClop

(chlorotripyrrolidinophosphonium hexafluorophosphate), HBTU (2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate), HATU (2-(7-aza-1H-benzotriazole-1-yl)-1,1,3,3,-tetramethyluronium hexafluorophosphate), HOSu (N-hydroxysuccinimide), TBTU (2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethylaminium tetrafluoroborate), T3P (propylphosphonic anhydride), BopCl (bis(2-oxo-3-oxazolidinyl)phosphonic chloride) or 3-Cl-1-pyridinium iodide [[are]] is used as ~~an activation~~ the reagent for activating the free C-terminus or a side chain carboxylic acid of the peptide carboxylic acid.

Claim 14 is **amended** as follows:

Claim 14. The method ~~Method~~ for the production of a substrate and subsequent reaction of this substrate with peptide cyclases into a cyclic peptide according to claim 10, wherein HOBt (N-hydroxybenzotriazole), HOAt (1-hydroxy-7-azabenzotriazole) or HONB (N-hydroxy-5-norbornene-2,3-dicarboxyiimide) [[are]] is used as [[a]] the coupling additive.

Claims 15 and 16 are **cancelled**.

Page 11, lines 5-23 of the specification is **amended** as follows:

As an alternative to the activation reagent DCC, the substrates according to the present invention can also be reacted by reaction of the peptide acid with the respective leaving group in the presence of other reagents activating the C-terminus of the peptide acid. Equivalents are known and can be used without leaving the area protected by the patent claims. Hereby, the

activation reagents known to persons skilled in the art include, for example, DCI (N,N-diisopropylcarbodiimide), PyClop (chlorotripyrrolidinophosphonium hexafluorophosphate), HBTU (2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate), HATU (2-(7-aza-1H-benzotriazole-1-yl)-1,1,3,3,-tetramethyluronium hexafluorophosphate), HOSu (N-hydroxysuccinimide), TBTU (2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethylaminium tetrafluoroborate), T3P (propylphosphonic anhydride), BopCl (bis(2-oxo-3-oxazolidinyl)phosphonic chloride) and 3-Cl-I- pyridiniumiodide. Apart from HOBt listed above, the substances HOAt (1-hydroxy-7-azabenzotriazole) and HONB (N-hydroxy-5-norbornene-2,3-dicarboxyiimide), which are known to persons skilled in the art, can also be used as coupling additives. It is known to persons skilled in the art that these reactions are effectively carried out with the addition of a base, such as e.g. DIPEA. Furthermore, different solvents for use in the methods mentioned are known to persons skilled in the art. Skilled persons can produce these combinations of activation reagents, coupling additives, bases, and solvents themselves with their general knowledge and standard literature.

The following is an examiner's statement of reasons for allowance:

The applicants have pointed out that the claims are restricted to charge-stabilized leaving groups which are defined in the description, on page 11, lines 25-33, as follows: "Charge-stabilized leaving groups are understood in the present invention to be chemical compounds which possess a thio or hydroxyl group and in which the free electron pair of the thiolate or hydroxylate ion released by the acylation reaction stands in conjugation with other electron pairs from, for example, but not exclusively, C=C or C=N double bonds or in which the thio or

hydroxyl group is bound to a carbon atom which is, for its part, bound to an aromatic or heteroaromatic ring." Since the scope of the charge-stabilized leaving groups is limited as such, the rejections under 35 U.S.C. 112, first paragraph and 35 U.S.C. 102(b) over Walsh (US 2002/0192773) have been withdrawn.

Furthermore, the applicants have provided a certified English translation of German patent application 103 35 584.7, thus perfecting the claim to priority to the German patent application. The perfected foreign priority filing date antedates the references Grunewald and Sieber. Therefore, the rejections under 35 U.S.C. 102(a) and 35 U.S.C. 103(a) over Grunewald and Sieber have been withdrawn.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571)272-3444. The examiner can normally be reached on Mon-Fri 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Allison M. Ford/
Primary Examiner, Art Unit 1653

Susan E Fernandez
Examiner
Art Unit 1651

sef